"DESIGN AND DEVELOPMENT OF NANOSPONGES FOR TOPICAL APPLICATION"

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By

Mr Updesh Lade

M.Pharm.

GUIDE

Dr Rajesh Mujariya

M.Pharm., PhD

INSTITUTE OF PHARMACEUTICAL SCIENCE AND RESEARCH

SARDAR PATEL UNIVERSITY, BALAGHAT (M.P.),

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1. INTRODUCTION

1. Introduction

The development of a wide spectrum of nanoscale technologies is beginning to change the foundations of disease diagnosis, treatment and prevention. Various nanodevices have had a significant impact on medical technology, greatly enhancing the efficacy of many existing drugs and enabling the construction of entirely new therapeutic modalities. Nanosponges are new class of materials with cavities of few nanometer dimensions into which wide variety of substances can be encapsulated These particles are capable of carrying both lipophilic and hydrophilic substances and of improving the solubility of poorly water soluble molecules.They revolutionize the treatment of various diseases and early trials suggest that this technology is five times more effective in targeting drugs to breast cancer cells than conventional methods. (Bolisetti S, 2012).

A Nanosponge is a size of virus with a scaffold structure of naturally degradable polyester. The long length polyester strands are mixed in solution with small molecules called cross-linkers that have an affinity for certain portions of the polyester. They ‘cross link’ segments of the polyester to form a spherical shape that has many pockets (or cavities) where drugs can be stored. The polyester is biodegradable i.e. breaks up in the body to release the drug on a known schedule. Nanosponges come under the class of encapsulating nanoparticles which encapsulate drug molecules within its core. These nanosponges represent a novel class of nanoparticles usually obtained by natural derivatives. As compared to the other nanoparticles, they are insoluble both in water and organic solvents, porous, nontoxic and stable at high temperatures up to 300°C. They have ability to capture, transport and selectively release a huge variety of substances because of their 3-dimensional structure containing cavities of nanometric size and tunable polarity. Furthermore, nanosponges show a remarkable advantage in comparison with the common nanoparticles: indeed, they can be easily regenerated by different treatments, such as washing with eco-compatible solvents, stripping with moderately inert hot gases, mild heating, or changing pH or ionic strength. For all these characteristics, nanosponges have been already employed in different applied fields, such as cosmetic and pharmaceutical sectors. (Bolisetti S, 2012).

1.1 Advantages of SLN ((Bolisetti S, 2012)

- Improve aqueous solubility of lipophilic drugs,
- To protect degradable molecules and to formulate drug delivery systems for various administration routes besides the oral one.
- The simple chemistry of polymers and cross linkers does not pose many problems in the preparation.
- They mix with water and are used as a transport fluid.
- They can be used to mask unpleasant flavors.
- The chemical linkers enable the nanosponges to bind preferentially to the target site.
- The engineering capacity of nanosponge is due to the relatively simple chemistry of its polyesters and cross-linking peptides, compared to many other nanoscale drug delivery

1.2 Synthesis of nanosponges : (Vishwakarma A, 2014)

It is one of the important criteria for the formation of product obtained activity in β-cyclodextrin, titanium oxide.

1) Solvent method:

The solvent required will be mix with the polymer mainly in a polar aprotic solvent for exampledimethylforamide, dimethylsulfoxide then add this mixture to cross linker in a exceed quantity, the ratio for cross linker/ molar ratio is preferred as 4 to 16. The reaction is proceed with a solvent reflux temperature and time ranging from 1 to 48 hr(21). The cross linkers which may preffered are dimethyl carbonate and carbonyl diimidazole. The reaction is completed and solution is allow to cool at room temperature then product is added to excess of bi-distilled water and product is recovered by filtration under vaccum and simultaneously purify by prolonged soxhlet extraction with ethanol. Finally product is dried under vaccum and grinded in a mechanical mill to obtain homogeneous powder.

2) Ultrasound assisted synthesis:

Nanosponges are obtained by reacting polymer with cross linkers without adding or without using solvent and sonification is maintained. The size obtained by this technique wil be spherical and uniform. The polymer is mix with a cross linkers in a balanced ratio in a flask. The flask is placed in a molar ratio in an ultrasound bath field with water and temperature

maintained at 90ºc. the mixture is sonicated for 5hr. Then the mixture is kept to cool and product is break roughly then the product is washed with water to remove non-reacted polymer and subsequently purified by soxhlet extraction with ethanol. The product is dried under vaccum at 25ºc until its further use is utilized.

3) Loading of drug into nanosponges:

Nanosponges obtained should be pretreated to maintain mean particle size blow 500nm. Nanosponges are suspended in water and were sonicated to avoid presence of aggregates and particles and got centrifuged to obtain colloidal fraction, then supernatant is separated and dried sample by freezing by drying. Further proceeding start with preparing aqueous suspension of nanosponges and excess amount of drug is dispensed for maintaining suspension under constant stirring for specific time period for complexation is over the undissolved drug (uncomplexed condition) is separated from complexed drug with the process of centrifugation. This process helps in evolving solid crystals of nanosponges by solvent evaporation or freeze drying. Nanosponges crystal play important part in complexation with drug. Para-crystalline nanosponges revealed different loading capacities when compared to crystalline nanosponges poorly crystalline nanosponges had act drug loading as a mechanical mixture rather than inclusion complex.

1.3 Factors Affecting the Formation of Topical Nano-Sponges (Preethi S, 2020)

Polymer

The nature of polymer affects the formation of Nanosponge. To form a complex cavity size of the polymer must be appropriate to include a drug molecule of a specific size. The particle size of the polymer should also be in nanometers size.

Drug molecule

For a drug molecule to form a complex with polymer, it must-have features like a molecular weight between 100 and 400. It must contain less than condensed rings, water solubility has to be less than 10mg/ml and the Melting point must be below 250◦

Temperature

As temperature increases, the magnitude of the apparent stability constants of the drug and polymer complex decreases. It might reduce interaction forces between drug and polymer.

Method of preparation

The effectiveness of the different method of preparation rely on the drug, polymer and cross-linker used. In most of the cases, it was found that freeze-drying is more effective than vacuum drying for drug and polymer complex.

Degree of substitution

The complexing capacity of Nano sponge depends on the number, position and type of the substituent on the parent drug and polymer molecule.

2. LITERATURE REVIEW

2.1 Priyanka D *et al* (2018) was studied the ibuprofen loaded nanosponges for topical application. Emulsion solvent diffusion method was selected to prepare ibuprofenloaded nanosponges using different ratios of drug:polymer. The obtained nanosponges have been evaluated for physicochemical characteristics and *in vitro* release studies.

2.2 Shoaib Q et al (2018) was studied nanosponge (NS) based sustained release formulations of naproxen (NAP) and ibuprofen (IBU). Six formulations of each candidate drug were prepared by emulsion solvent diffusion method, using varying ratios of polymers, i.e., ethyl cellulose and polyvinyl alcohol. The prepared formulations were evaluated for various parameters including production yield, particle size, polydispersity index, actual drug content and entrapment efficiency. Morphological, structural and thermo-analytical evaluations were performed using various techniques. In vitro release studies were performed on selected formulations.

2.3 Penjuri SCB *et al* (2016) was studied the Lansoprazole loaded nanosponges by Emulsion solvent diffusion method using ethylcellulose, PVA and pluronic F-68 and dichloromethane as a solvent. The prepared nanosponges was evaluated for percentage yield, incorporation efficiency, particle size, drug polymer compatibility, scanning electron microscopy and *invitro* drug release. SEM studies confirmed their porous structure with number of nanochannels. The FTIR spectra showed stable character of lansoprazole in mixture of polymers and revealed the absence of drug polymer interactions. DSC study revealed that drug was involved in complexation with nanosponges.

2.4 Srinivas P *et al* (2013) was studied the controlled release Voriconazole Nanosponges for topical and oral delivery. Nanosponges using three different polymers ethyl cellulose, Poly (methyl methacrylate) and Pluronic F-68 (poloxamer 188) was prepared successfully using PVA as surfactant by emulsion solvent evaporation method. The effects of different drug: polymer ratios, surfactant concentration, stirring speeds and time, sonication time on the physical characteristics of the

nanosponges as well as the drug entrapment efficiency of the nanosponges were investigated. Particle size analysis and surface morphology of nanosponges were performed. The scanning electron microscopy of nanosponges showed that they were spherical in shape and spongy in nature. The particle size of the optimized formulations was in the range of 200-400nm and the drug entrapment efficiency was found to be in the range of 69.8 % to 72.5%.

3. AIM AND OBJECTIVE

3.1 Aim

To Design and develop Nanosponges for Topical Application.

3.2 Objective

1. To provide prolonged and constant therapeutic effect.
2. To reduce the dosing frequency and therefore improve the patient compliance
3. To Decrease in toxicity while maintaining therapeutic effects.
4. To provide controlled, sustained and targeted delivery of the drug.
5. Development of safe medicine.

4. PLAN OF WORK

4.1. Literature survey

4.2. Procurement of Drugs and Excipients

4.3. Preformulation study

- Physical Characteristics
- Melting Point
- Solubility studies

4.4. Formulation of Nanosponges by Emulsion solvent diffusion method.

4.6. Evaluation of Nanosponges

a) Surface characterisitics by SEM

b) Drug-Polymer interaction study using FTIR

c) Percentage yield

d) Entrapment efficiency

e) *In vitro* drug release profile

4.7 Results and Discussion

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(Mr Updesh Lade)
M.Pharm.
Research Scholar

(Dr Rajesh Mujariya)
M.Pharm., PhD
Research Guide